

K1532

I

II

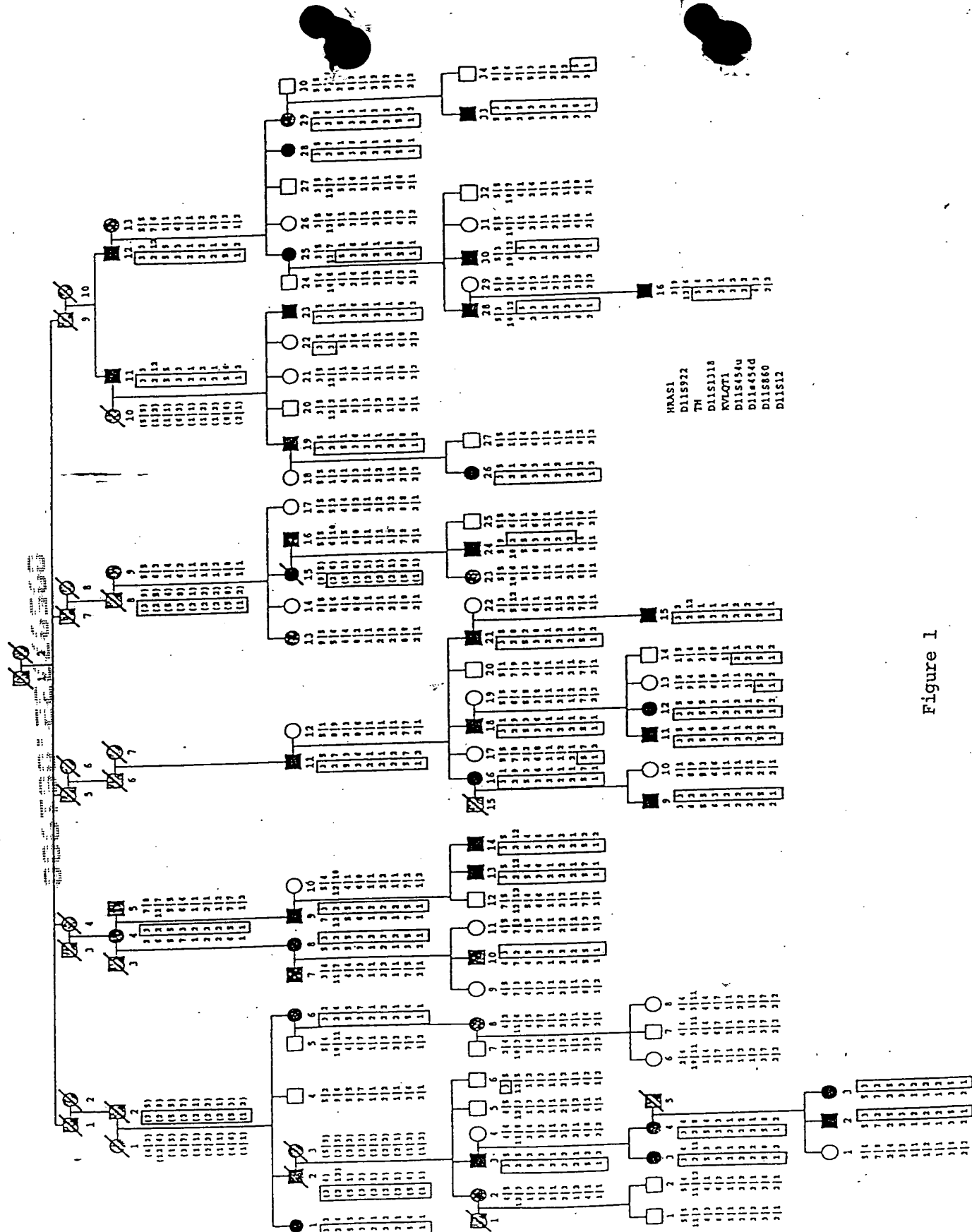
III

IV

V

VI

VII



HRAS1  
DI15922  
TH  
DI151318  
KVLOT1  
DI154340  
DI145340  
DI15860  
DI1512

Figure 1

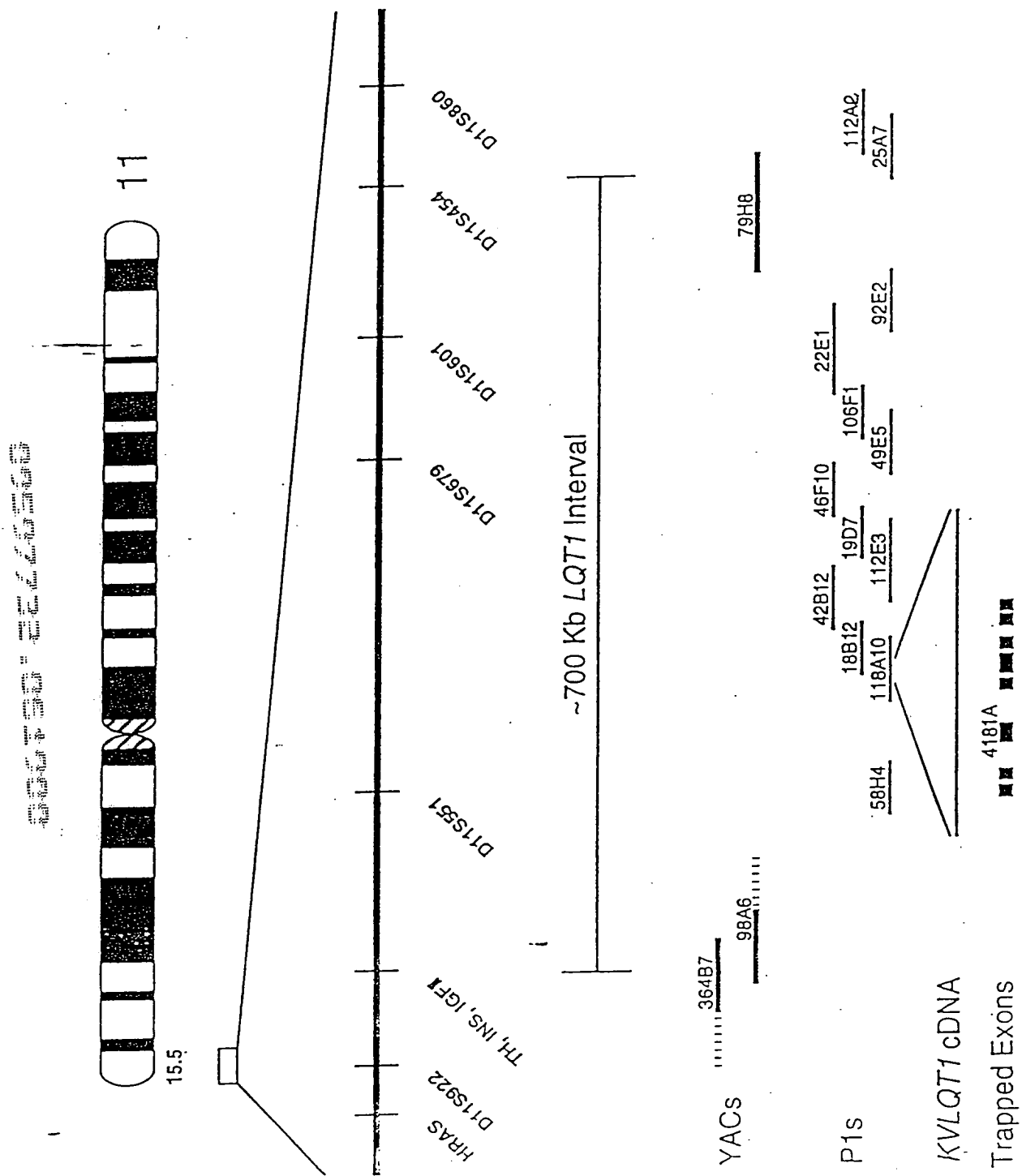


Figure 2

[illegible][illegible]

Figure 3

3.2 kb →

Heart  
Brain  
Placenta  
Lung  
Liver  
Skeletal muscle  
Kidney  
Pancreas

Figure 4

CTGCCCCCTCCGGCCCCGCCCCGAGCGCCCGGGCTGGGCCGGCAGCGCCCCCGCGGGGGCTGGCAGCAGTGGCTGCC-81  
 CGCACTGCGCCCCGGGCGCTCGCCTTCGCTGCAGCTCCCGTGCCGCCCGCTCGGGCCGGCCCCCGGCAGGCCCTCCTCGTT-162  
 ATGCGCCGCGCCTCCTCCCCGCCCAGGGCCGAGAGGAAGCGCTGGGGTTGGGGCCGCTGCCAGGCGCCCGGGGGGAGC-243  
 M A A A S S P P R A E R K R W G W G R L P G A R R G S -27  
 GCGGGCTGGCCAAGAAGTGGCCCTTCTCGCTGGAGCTGGCGGAGGGCGGCCCGGGCGGGCGCGCTCTACGCGCCCATC-324  
 A G L A K K C P F S L E L A E G G P A G G A L Y A P I -54  
 GCGCCCGGCGCCCCAGGTCCCCGCGCCCCCTGCGTCCCCGGCCGCGCCCCCGCGCCCCCAGTTGCTTCCGACCTTGGCCCG-405  
 A P G A P G P A P P A S P A A P A A P P V A S D L G P -81  
 CGGCCCGCGGTGAGCCTAGACCCGCGCGTCTCCATCTACAGCACGCGCCCGCCGGTGTGGCGCGCACCCACGTCCAGGGC-486  
 R P P V S L D P R V S I Y S T R R P V L A R T H V Q G -108  
 CGCGTCTACAACCTCCTCGAGCGTCCCACCGGTGGAAATGCTTCGTTTACCACTTCGCCGTCTCCTCATCGTCTGGTC-567  
 R V Y N F L E R P T G W K C F V Y H F A V F L I V L V -135  
 TGCCTCATCTTCAGCGTGTGTCCACCATCGAGCAGTATGCCGCCCTGGCCACGGGACTCTCTTCTGGATGGAGATCGTG-648  
 C L I F S V L S T I E Q Y A A L A T G T L F W M E I V -162  
 CTGGTGGTGTCTTCTCGGGACGGAGTACGTGGTCCGCCTCTGGTCCGCGGGCTGCCGCGAGCAAGTACGTGGGCTCTGGGG-729  
 L V V F E G T E Y V V R L W S A G C R S K Y V G L W G -189  
 CGGCTGCGCTTTGCCCCGAAGCCCATTTCCATCATCGACCTCATCGTGGTGTGGCTCCATGGTGGTCTCTGCGTGGGC-810  
 R L R F A R K P I S I I D L I V V V A S M V V L C V G -216  
 TCCAAGGGGCGAGTGTTCGCCACGTGGCCATCAGGGGCATCCGCTTCCTGCAGATCCTGAGGATGCTACACGTGACCGC-891  
 S K G Q V F A T S A I R G I R F L O I L R M L H V D R -243  
 CAGGGAGGCACCTGGAGGCTCCTGGGCTCCGTGGTCTTCATCCACGCCAGGAGCTGATAACCACCCTGTACATCGGCTTC-972  
 Q G G T W R L L G S V V F I H R Q E L I T T L Y I G F -270  
 CTGGGCTCATCTTCTCCTCGTACTTTGTGTACCTGGCTGAGAAGGACGCGGTGAACGAGTCAGGCCGCGTGGAGTTCCGGC-1053  
 L I G L I F S S Y F V Y L A E K D A V N E S G R V E F G -297  
 AGGTACGCAGATGCGCTGTGGTGGGGGTGGTTCACAGTCACCACCATCGGCTATGGGGACAAGGTGCCCCAGACGTGGGTC-1134  
 S Y A D A L W W G V V T V T T I G Y G D K V P Q T W V -324  
 GGAAGACCATCGCCTCCTGCTTCTGTCTTTGCCATCTCCTTCTTTGCGCTCCCAGCGGGATTCTTGGCTCGGGGTTT-1215  
 G K T I A S C F S V F A I S F F A L P A G I L G S G F -351  
 GCCCTGAAGGTGCAGCAGAAGCAGAGGCAGAAGCACTTCAACCGGCAGATCCCGGCGGCAGCCTCACTCATTCAGACCGCA-1296  
 A L K V Q Q K Q R Q K H F N R Q I P A A A S L I Q T A -378  
 TGCAGGTGCTATGCTGCCGAGAACCCCGACTCCTCCACCTGGAAGATCTACATCCGGAAGGCCCCCGGAGCCACACTCTG-1377  
 W R C Y A A E N P D S S T W K I Y I R K A P R S H T L -405  
 CTGTACCCAGCCCCAAACCCAAGAAGTCTGTGGTGGTAAAGAAAAAAGTTCAAGCTGGACAAAGACAATGGGGTGA-1458  
 L S P S P K P K K S V V V K K K K F K L D K D N G V T -432  
 CCTGGAGAGAAGATGCTCACAGTCCCCCATATCACGTGCGACCCCCCAGAAGAGCGGCGGCTGGACCACTTCTCTGTGCGAC-1539  
 P G E K M L T V P H I T C D P P E E R R L D H F S V D -459  
 GGCTATGACAGTTCTGTAAGGAAGAGCCCAACACTGCTGGAAGTGAGCATGCCCATTTTCATGAGAACCAACAGCTTCGCC-1620  
 G Y D S S V R K S P T L L E V S M P H F M R T N S F A -486  
 GAGGACCTGGACCTGGAAGGGGAGACTCTGCTGACACCCATCACCCACATCTCACAGCTGCGGGAACACCATCGGGCCACC-1701  
 E D L D L E G E T L L T P I T H I S Q L R E H H R A T -513  
 ATTAAGGTCATTGACGCATGCACTACTTTGTGGCCAAGAAGAAATTCCAGCAAGCGCGGAAGCCTTACGATGTGCGGGAC-1782  
 I K V I R R M Q Y F V A K K K F Q Q A R K P Y D V R D -540  
 GTCATTGAGCAGTACTCGCAGGGCCACCTCAACCTCATGGTGGCATCAAGGAGCTGCAGAGGAGGCTGGACCACTTCATT-1863  
 V I E Q Y S Q G H L N L M V R I K E L Q R R L D Q S I -567

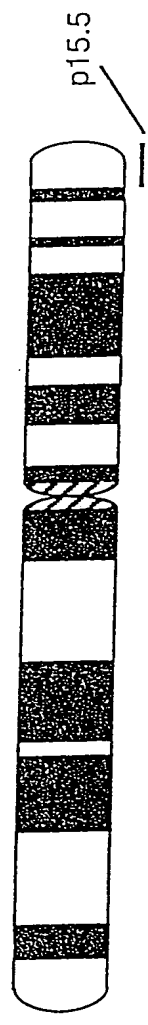
Figure 5A

GGAAGCCCTCACTGTTTCATCTCCGTCTCAGAAAAGAGCAAGGATCGCGGCAGCAACACGATCGGGCGCCCGCTGAACCGA-1944  
 G K P S L F I S V S E K S R D R G S N T I G A R L N R -594  
 GTAGAAGACAAGGTGACGCAGCTGGACCAGAGGCTGGCACTCATCACCGACATGCTTACCAGCTGCTCTCCTTGCACGGT-2025  
 V E D K V T Q L D Q R L A L I T D M L H Q L L S L H G -621  
 GGCAGCACCCCCGGCAGCGGGCGGCCCCCAGAGAGGGCGGGGCCACATCACCCAGCCCTGCGGCAGTGGCGGCTCCGTC-2106  
 G S T P G S G G P P R E G G A H I T Q P C G S G G S V -648  
 GACCTGAGCTCTTCCTGCCAGCAACACCCTGCCACCTACGAGCAGCTGACCGTGCCAGGAGGGGGCCCGATGAGGGG-2187  
 D P E L F L P S N T L P T Y E Q L T V P R R G P D E G -675  
 TCCTGAGGAGGGGATGGGGCTGGGGGATGGGCCTGAGTGAGAGGGGAGGCCAAGAGTGGCCCCACCTGGCCCTCTCTGAAG-2268  
 S \* -676  
 GAGGCCACCTCCTAAAAGGCCAGAGAGAAGAGCCCCACTCTCAGAGGCCCAATACCCCATGGACCATGCTGTCTGGCAC-2349  
 AGCCTGCACTTGGGGGCTCAGCAAGGCCACCTCTTCCTGGCCGGTGTGGGGGCCCCGTCTCAGGTCTGAGTTGTTACCCCA-2430  
 AGCGCCCTGGCCCCCACATGGTGATGTTGACATCACTGGCATGGTGGTTGGGACCCAGTGGCAGGGCACAGGGCCTGGCCC-2511  
 ATGTATGGCCAGGAAGTAGCACAGGCTGAGTGCAGGCCCCACCTGCTTGGCCCAGGGGGCTTCCTGAGGGGAGACAGAGCA-2592  
 ACCCTGGACCCACGCTCAAATCCAGGACCCTGCCAGGCACAGGCAGGGCAGGACCAGCCACGCTGACTACAGGGCCAC-2673  
 CGGCAATAAAAAGCCCAGGAGCCCATTTGGAGGGCCTGGGCCTGGCTCCCTCACTCTCAGGAAATGCTGACCCATGGGCAGG-2754  
 AGACTGTGGAGACTGCTCCTGAGCCCCCAGCTTCCAGCAGGAGGGACAGTCTCACCATTTCCTCCAGGGCACGTGGTTGAGT-2835  
 GGGGGGAACGCCCACCTTCCTGGGTAGACTGCCAGCTCTTCCTAGCTGGAGAGGAGCCCTGCCTCTCCGCCCCCTGAGCCC-2916  
 ACTGTGCGTGGGGCTCCCGCCTCCAACCCCTCGCCAGTCCCAGCAGCCAGCCAAACACACAGAAGGGGACTGCCACCTCC-2997  
 CCTTGCCAGCTGCTGAGCCGAGAGAAGTGACGGTTCTACACAGGACAGGGGTTCTTCTGGGCATTACATCGCATAGAA-3078  
 ATCAATAATTTGTGGTGATTGATCTGTGTTTAAATGAGTTTCACAGTGTGATTTGATTATTAATGTGCAAGCTTTTC-3159  
 CTAATAAACGTGGAGAATCAC (A)n -3180

Figure 5B

118A10 42B12 19D7 46F10 49E5

chromosome 11



~400 kb

118A10

42B12

19D7

49E5

cos1

18B12

112E3

46F10

genomic clones

1 2 3 4 5 6 7 8 9 10

11 12 13 14 15 16

KVLTQ1 exons

Figure 6

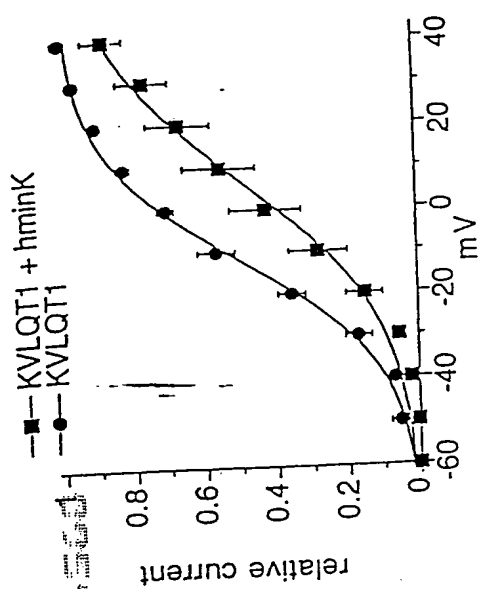


Figure 7A

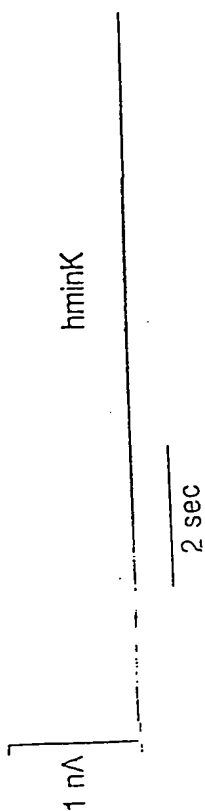


Figure 7B

Figure 7C

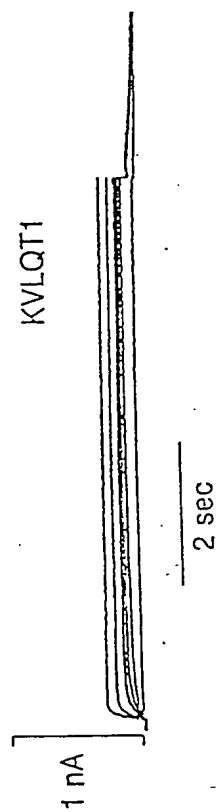


Figure 7D

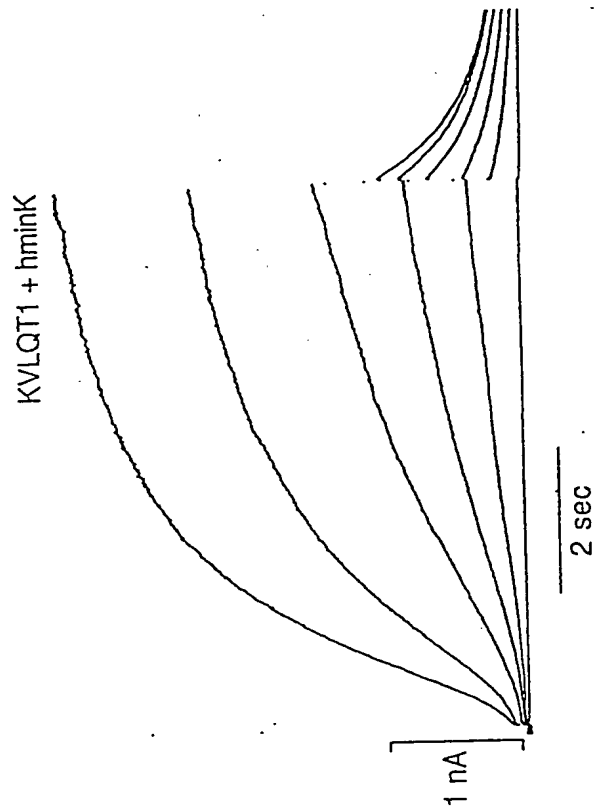


Figure 7E

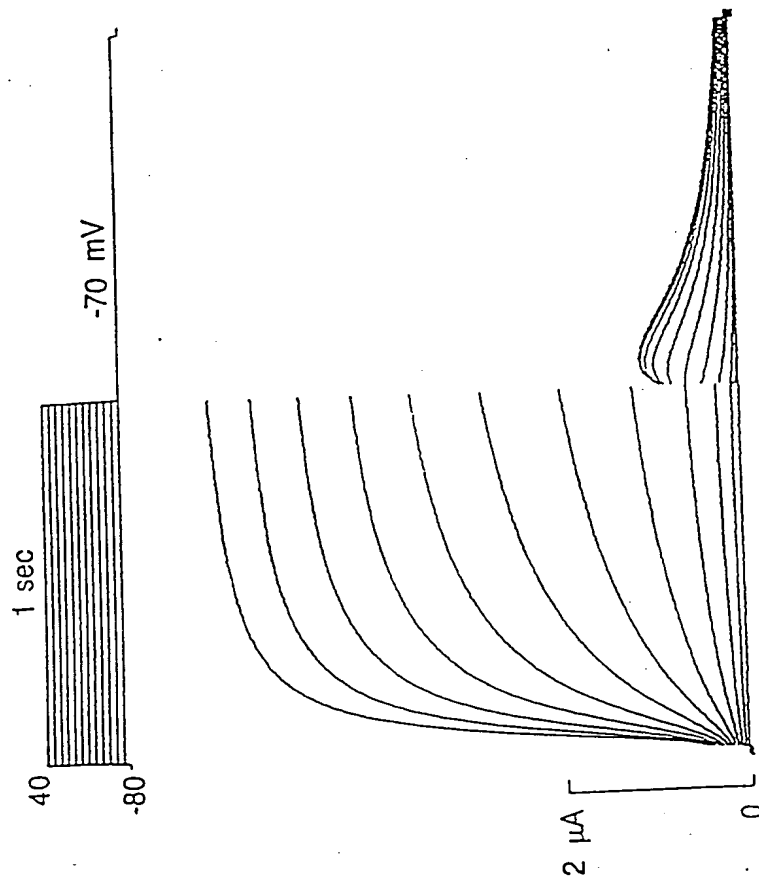


Figure 8A

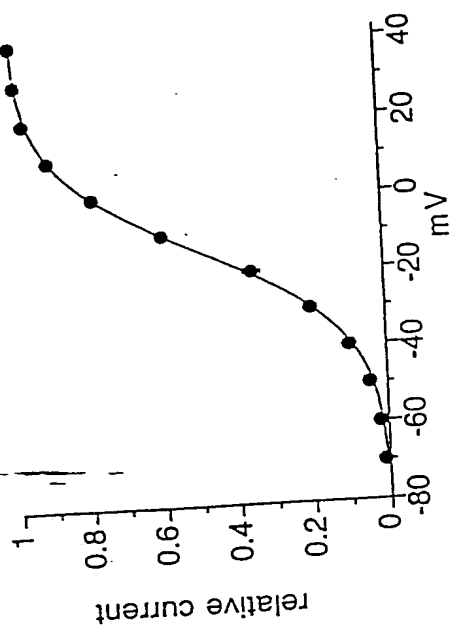


Figure 8B

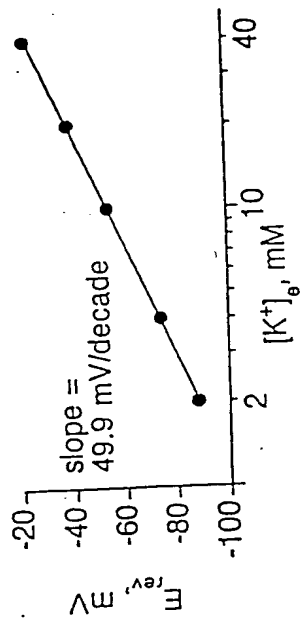


Figure 8C

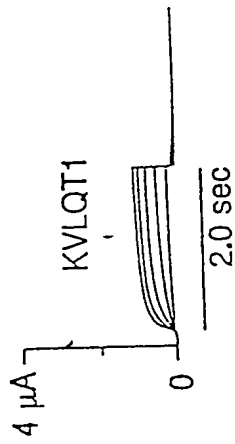


Figure 9A

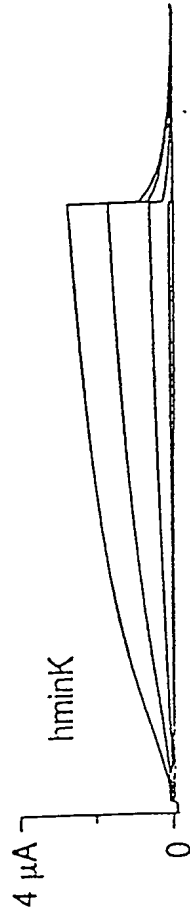


Figure 9B

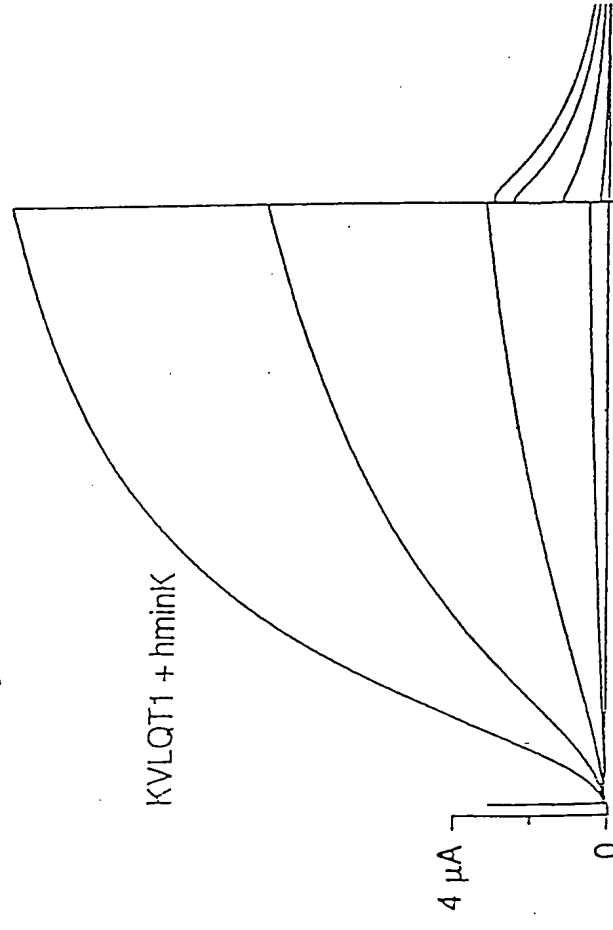


Figure 9C

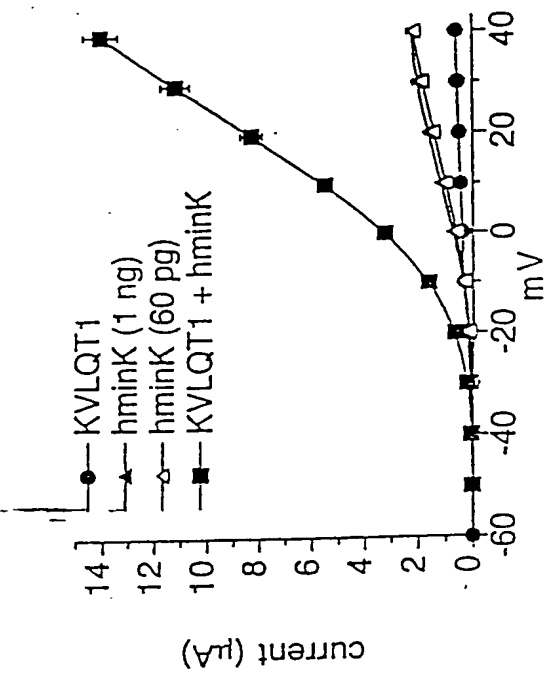


Figure 9D

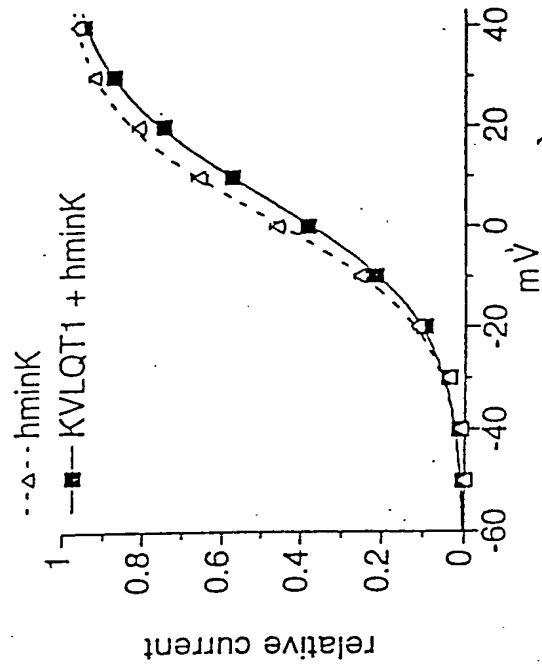


Figure 9E

Xenopus MNENAINSLYEAIPLPDGSSNGQRQEDRQANSFELKRETLVATDPPRPT

Human QGRVYNFLERPTGWKCFVYHFAVFLIVL  
 |||||

Xenopus INLDPRVSIYSGRRPLFSRTNIQGRVYNFLERPTGWKCFVYHFTVFLIVL

S1 S2  
 Human VCLIFSVLSTIEQYAALATGTLFWMEIVLVVFFGTEYVVRWSAGCRSKY  
 |||||

Xenopus ICLIFSVLSTIQYNNLATETLEWMEIVLVVFFGAEYVVRWSAGCRSKY

S3 S4  
 Human VGLWGRLRFARKPISIDLVVVASMVVLCVSGKQVFATSAIRGIRFLQ  
 |||||

Xenopus VGVWGRLRFARKPISVIDLVVVASVIVLCVGSNGQVFATSAIRGIRFLQ

S5  
 Human ILRMLHVDRQGGTWRLIGSVFIHRQELITTLYIGFLGLIFSSYFVYLAE  
 |||||

Xenopus ILRMLHVDRQGGTWRLIGSVFIHRQELITTLYIGFLGLIFSSYFVYLAE

Pore  
 Human KDAVNESGRVEFGSYADALWVGVTVTITIGYGDKVPQTWVGKTIASCFSV  
 |||||

Xenopus KDAIDSSGEYQFGSYADALWVGVTVTITIGYGDKVPQTWIGKTIASCFSV

S6  
 Human FAISFFALPAGILGSGFALKVQQKQKQKHFNRIQAAASLIQTAWRCYAA  
 |||||

Xenopus FAISFFALPAGILGSGFALKVQQKQKQKHFNRIQAAASLIQTAWRCYAA

Human ENPDSSTWKIYIRKAPRSHTLLSPSPKPKSVVVKKKFKLDDKONGVTPG  
 |||||

Xenopus ENPD SATWKIYIRKQSRNHIMSPSP

Human EKMLTVPHITCDPPEERRLDHFSVDGYDSSVRKSPITLLEVSMPHFMRNS

Human FAEDLDLEGETLLTPITHISQLREHHRATIKVIRRMQYFVAKKKFQQARK

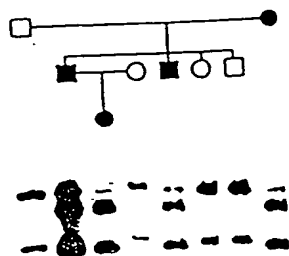
Human PYDVRDVIEQYSQGHNLNMRVIKELQRRLDQSIGKPSLFI SVSEKSKDRG

Human SNTIGARLNRVEDKVTQLDQRLALITDMLHQLLSLHGGSTPGSGGPPREG

Human GAHITQPCGSGGSVDPELFLPSNTLPTYEQLTVPRRGPDEGS

Figure 10

K1532



K2605

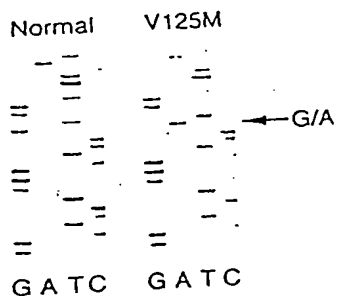
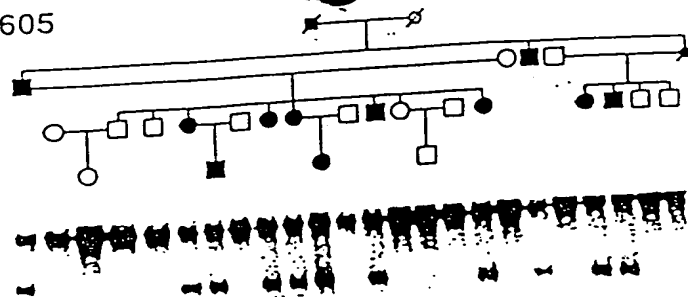


Figure 11A

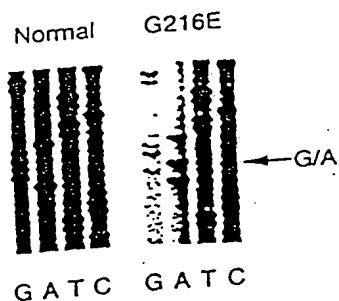
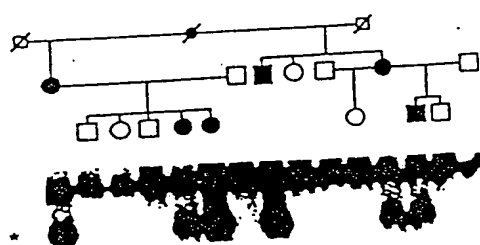


Figure 11B

K1723



K1807

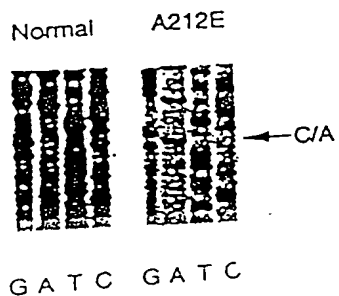
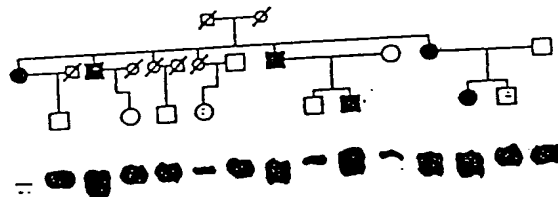


Figure 11C

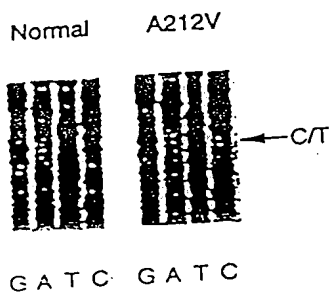


Figure 11D

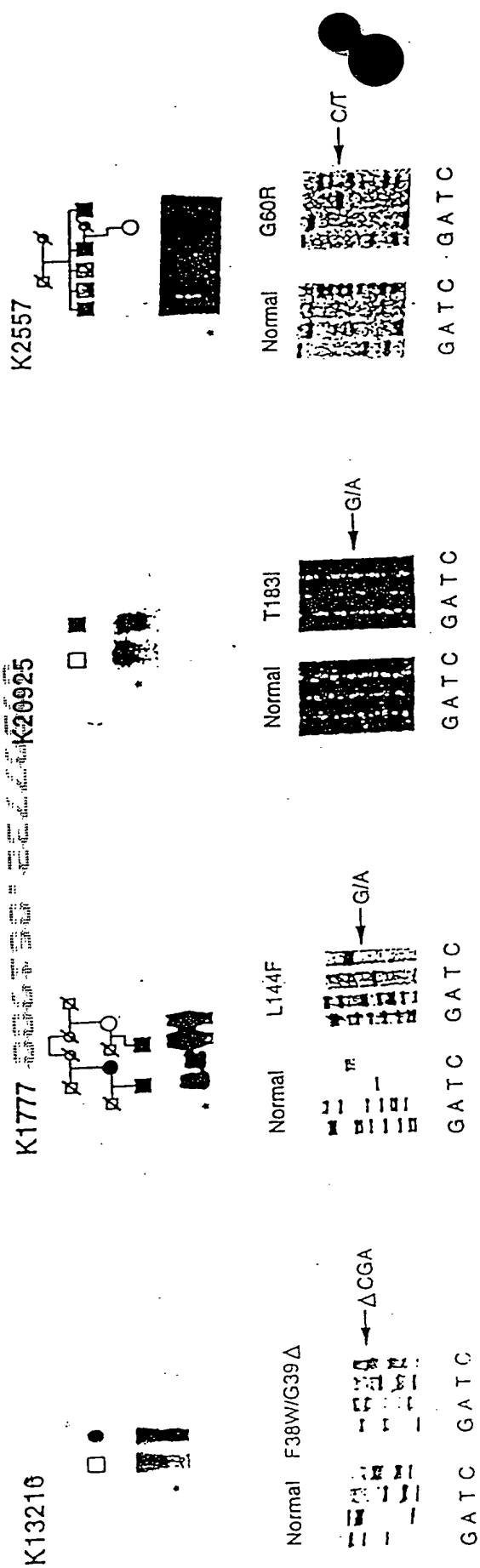


Figure 12A

Figure 12B

Figure 12C

Figure 12D

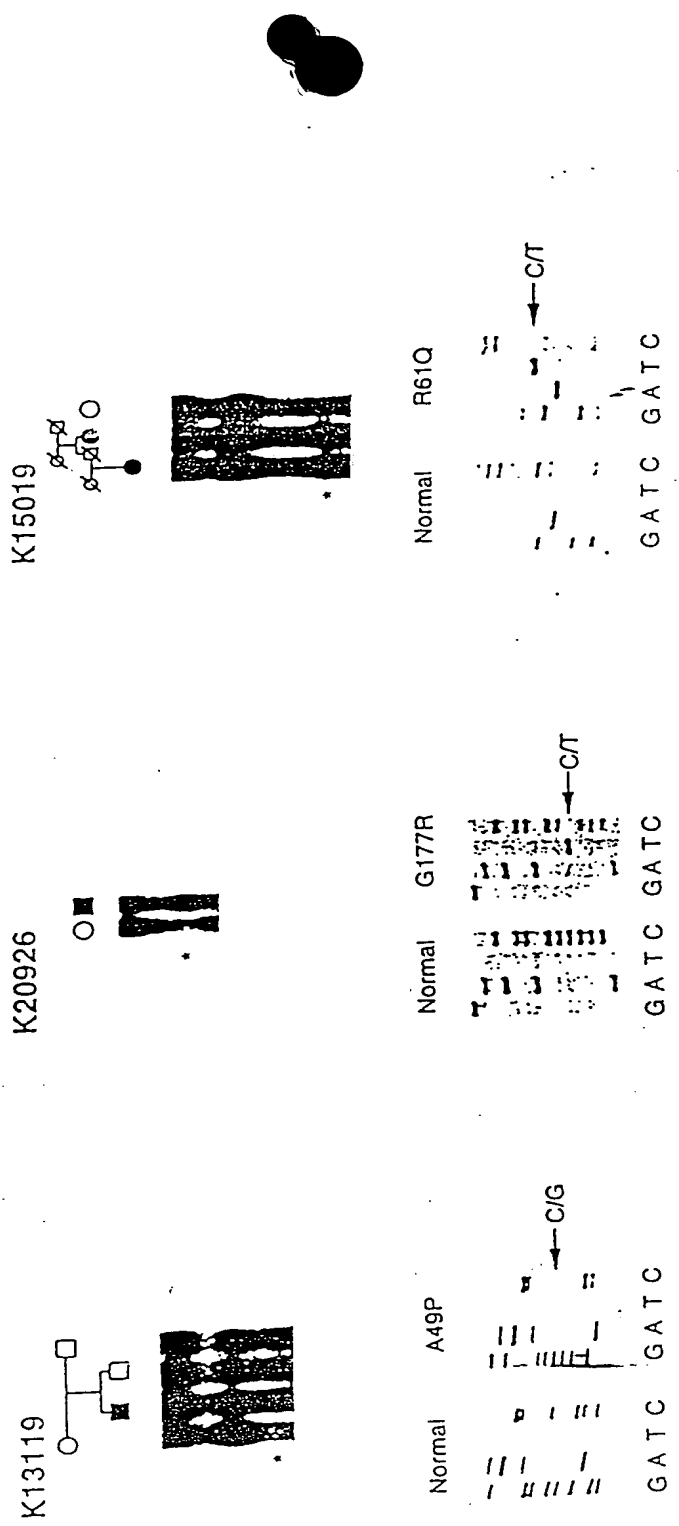
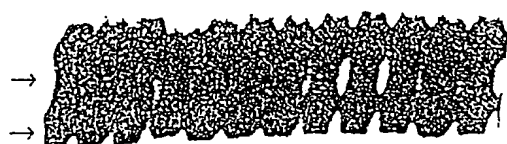
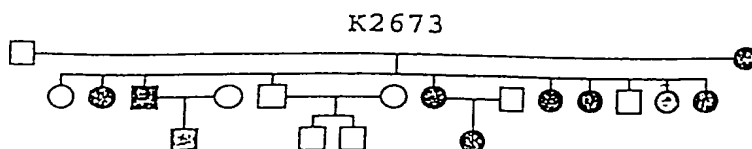
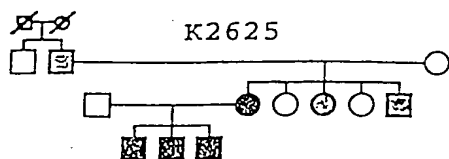


Figure 12E

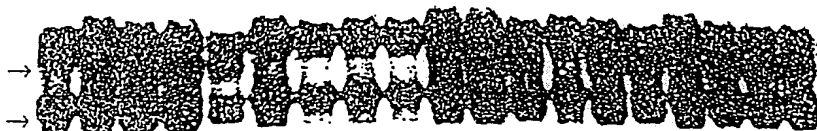
Figure 12F

Figure 12G



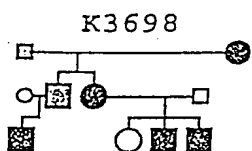
Gly168Arg

Figure 12H



Gly168Arg

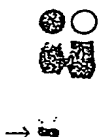
Figure 12I



Gly168Arg

Figure 12J

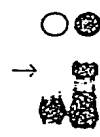
K19187



Gly314Ser

Figure 12K

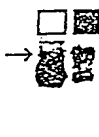
K22709



Tyr315Cys

Figure 12L

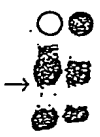
K2762



Lys318Asn

Figure 12M

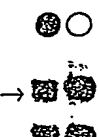
K3401



Leu353Pro

Figure 12N

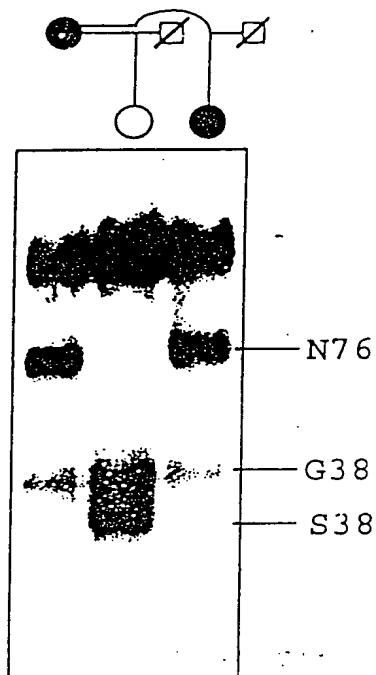
K2824



Arg366Trp

Figure 12O

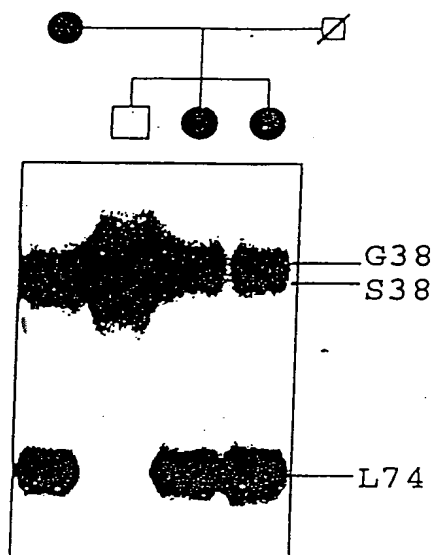
K1789



Normal	CAC	TCG	AAC	GAC	CCA	TTC	AAC
	H	S	N	D	P	F	N
				↓			
Mutant	CAC	TCG	AAC	AAC	CCA	TTC	AAC
	H	S	N	N	P	F	N

Figure 13A

K1754



Normal	CTG	GAG	CAC	TCG	AAC	GAC	CCA
	L	E	H	S	N	D	P
				↓			
Mutant	CTG	GAG	CAC	TTG	AAC	GAC	CCA
	L	E	H	L	N	D	P

Figure 13B

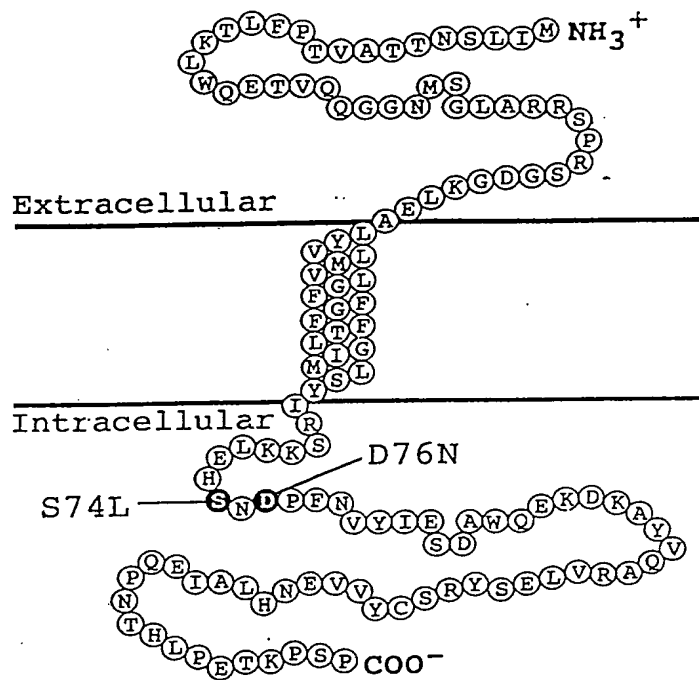


Figure 13C

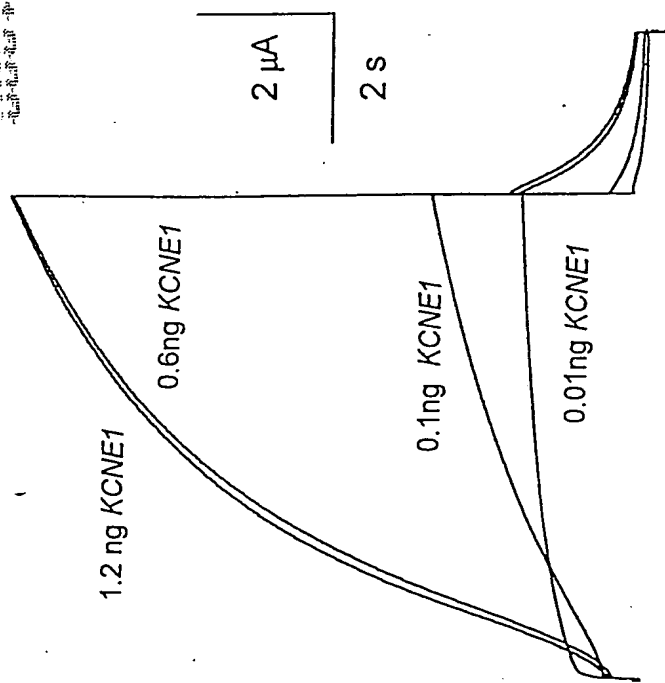


Figure 14A

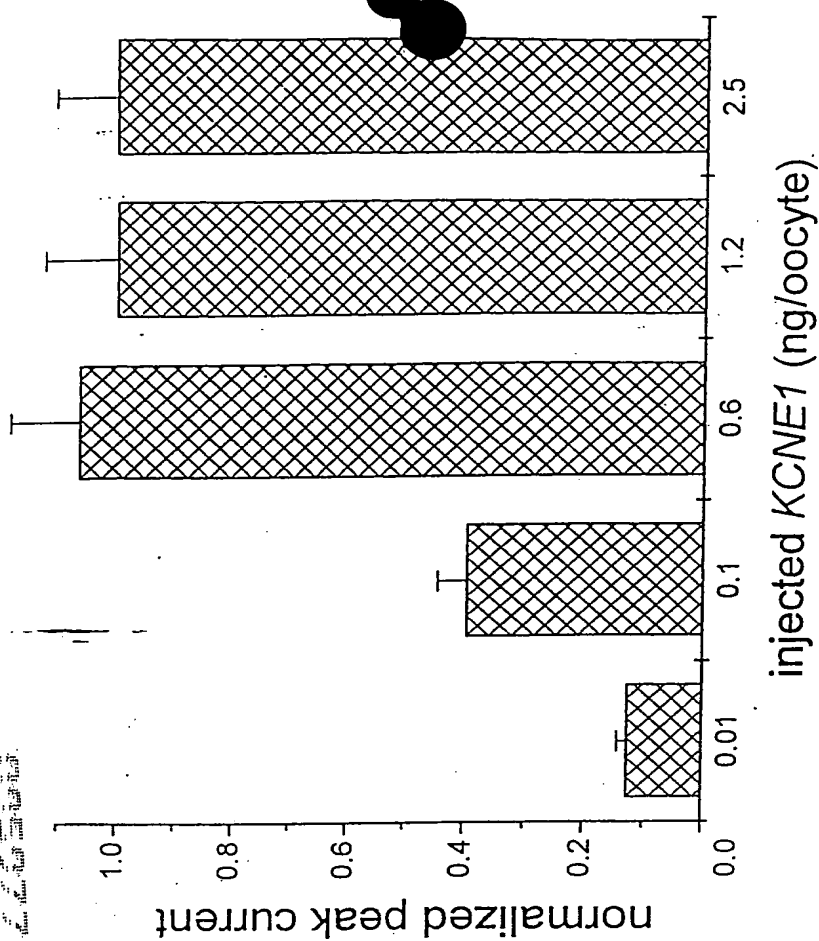


Figure 14B

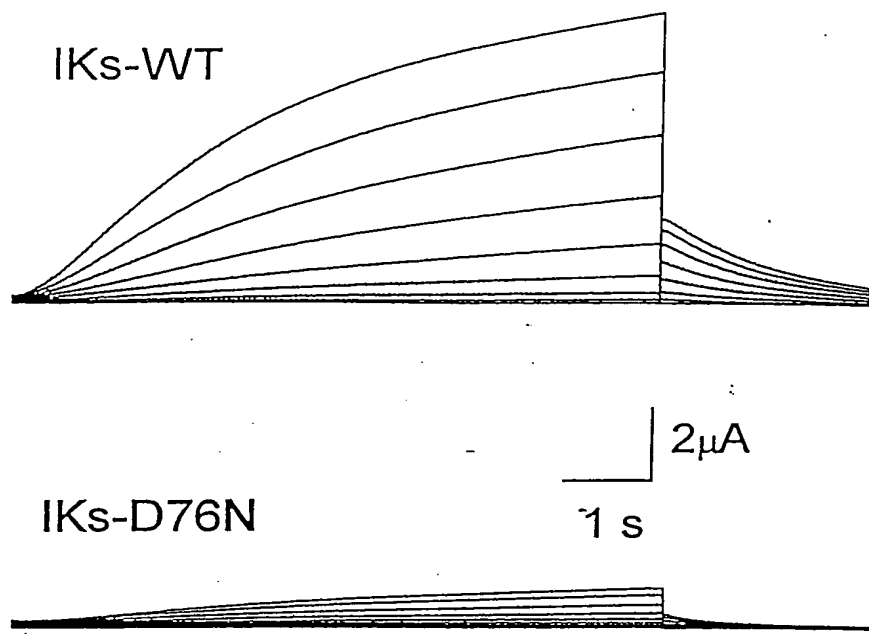


Figure 15A

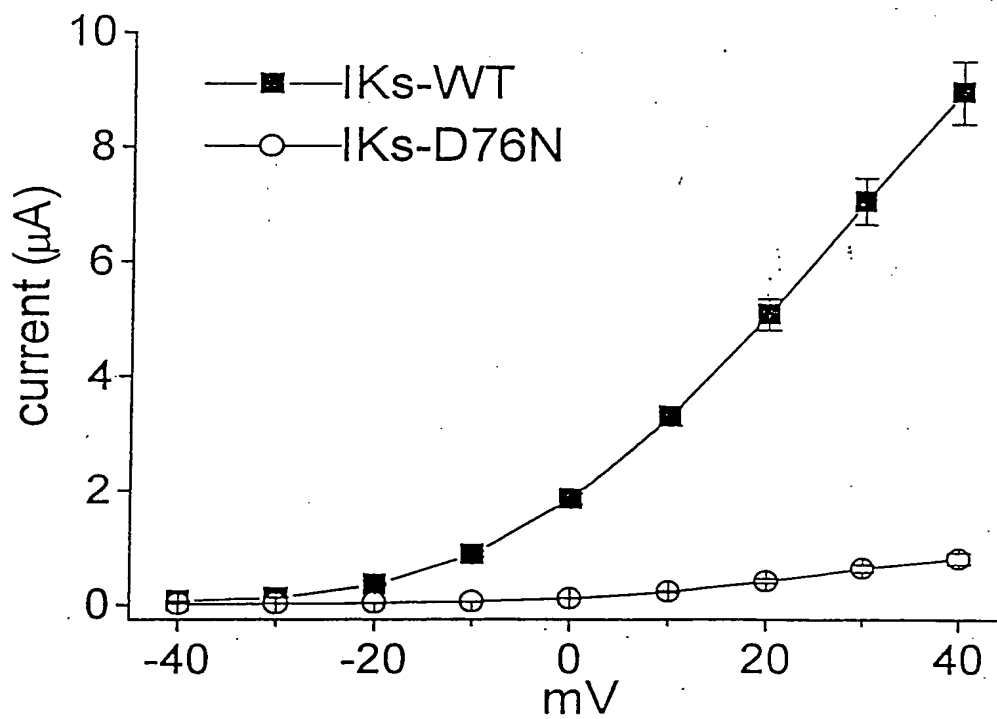


Figure 15B

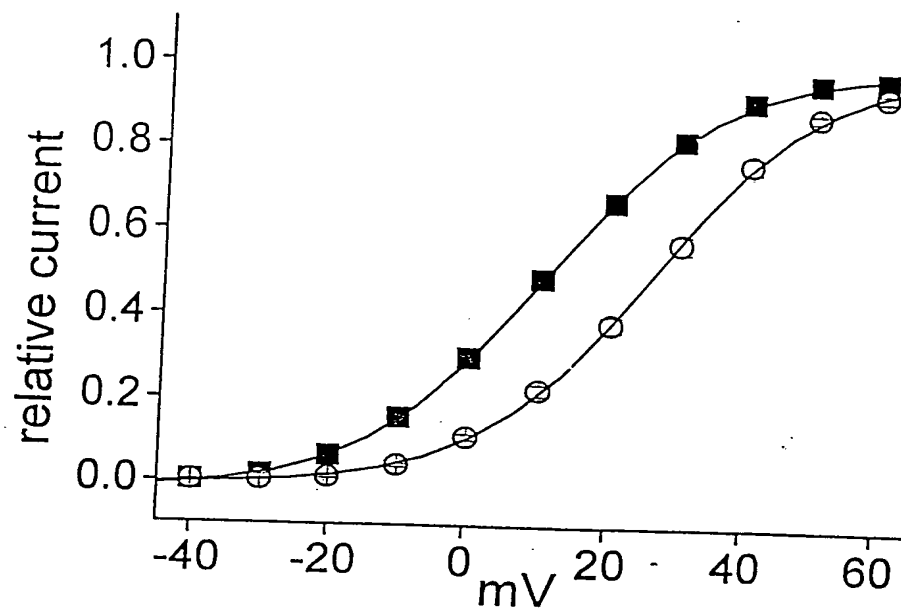


Figure 15C

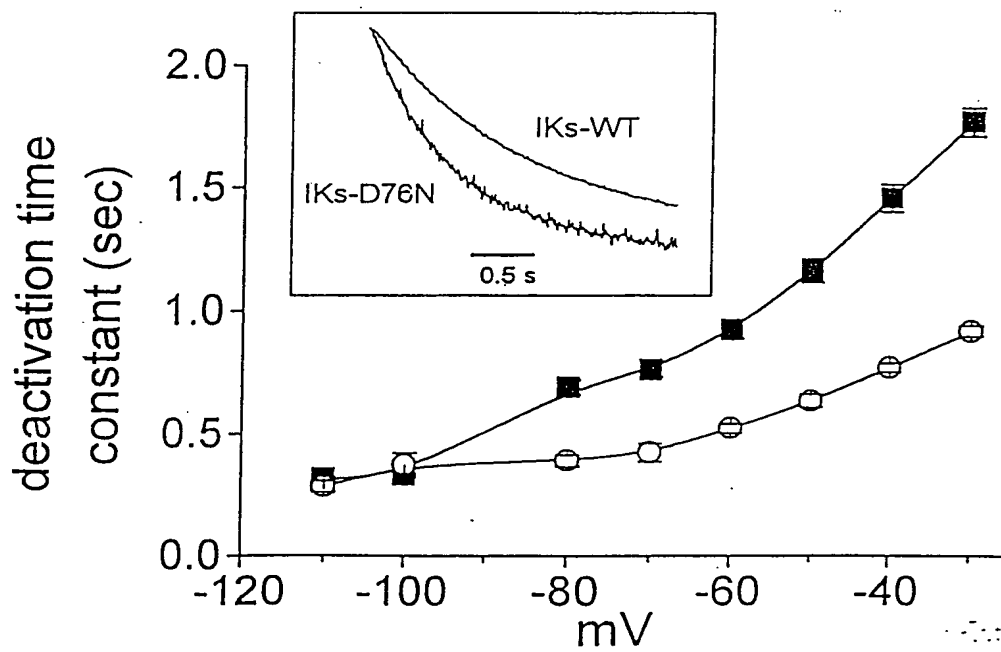


Figure 15D

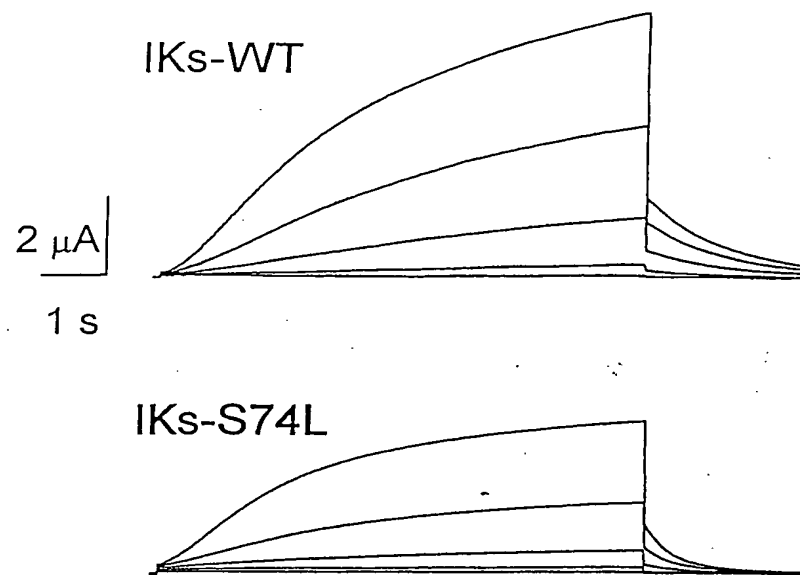


Figure 16A

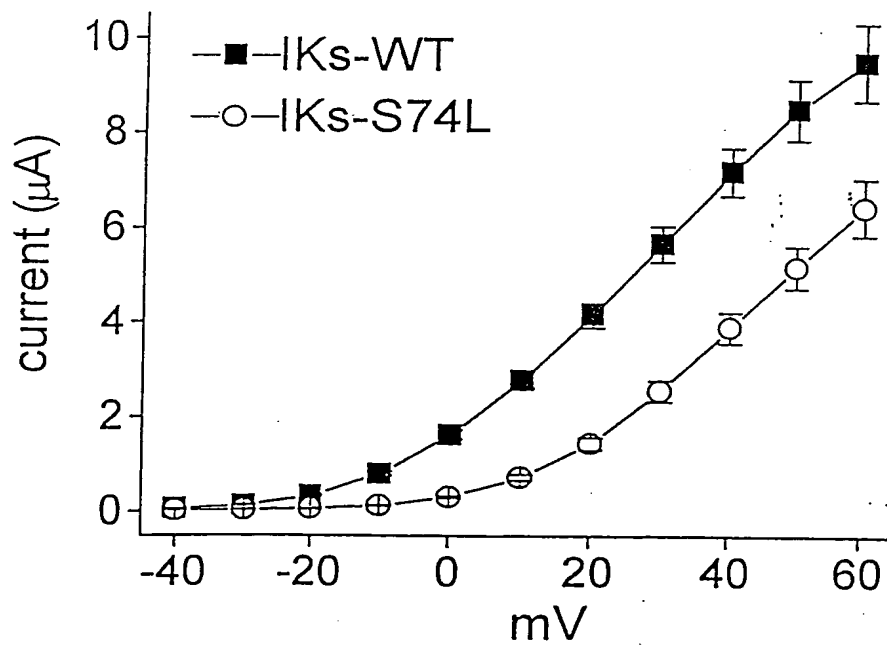


Figure 16B

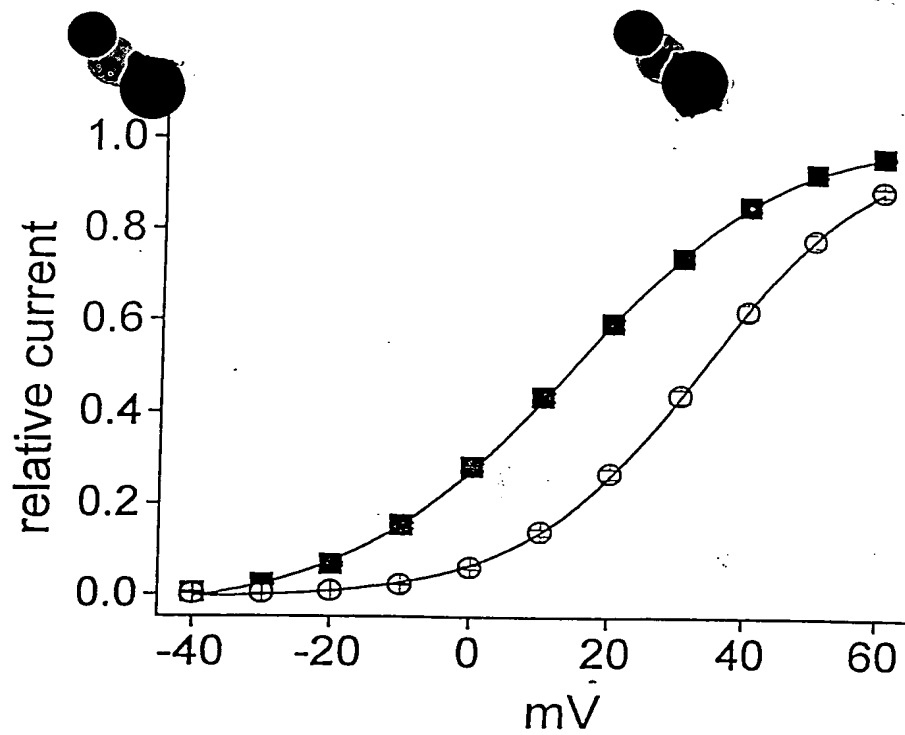


Figure 16C

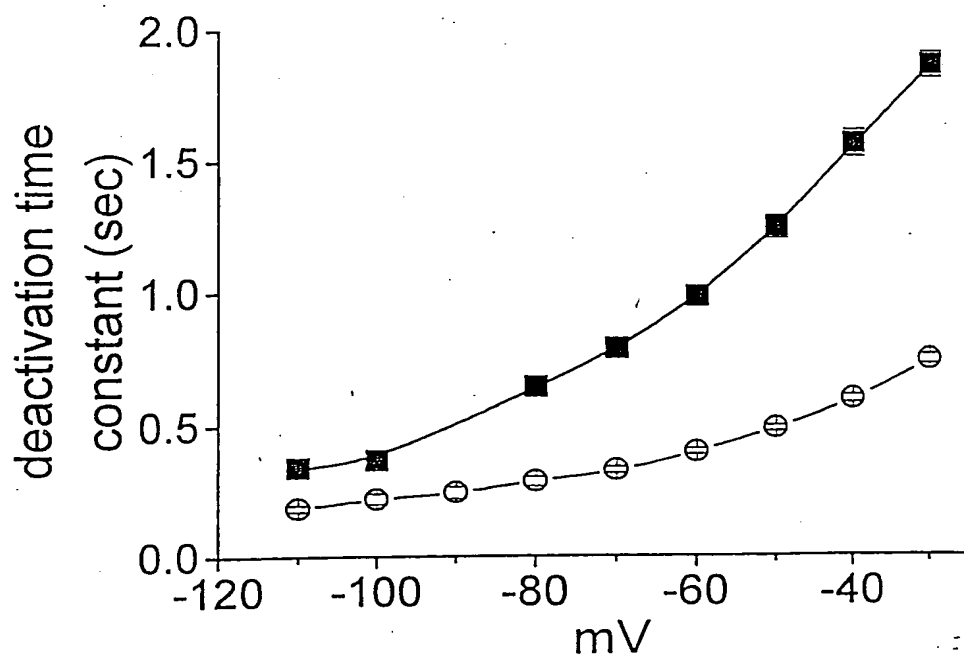


Figure 16D

q22.1-q22.2

chromosome 21



~60 kb

cos2

cos1

genomic clones

KCNE1 exons

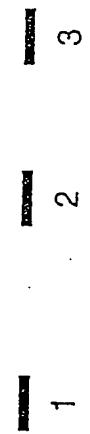


Figure 17

ACACCCGGCTCTCTCGGCATCTCAGACCCGGGAAAAATCCTCTGCTTTCTCTGGCCAGTTTCACACAATCATCAGGTGAG-81  
 CCCGAGGATCCATTGGAGGAAGGCATTATCTGTATCCAGAGGAAATAGCCAAGGATATTTCAGAGGTGTGCCTGGGAAGTTTG-162  
 AGCTGCAGCAGTGGAACCTTAATGCCCAGGATGATCCTGTCTAACACCACAGCGGTGACGCCCTTTCTGACCAAGCTGTGG-243  
 M I L S N T T A V T P F L T K L W -17  
 CAGGAGACAGTTTCAGCAGGGTGGCAACATGTCGGGCTGGCCCGCAGGTCCCCCGCAGCGGTGACGGCAAGCTGGAGGCC-324  
 Q E T V Q Q G G N M S G L A R R S P R S G D G K L E A -44  
 CTCTACGTCTCATGGTACTGGGATTTCTTCGGCTTCTTCACCCTGGGCATCATGCTGAGCTACATCCGCTCCAAGAAGCTG-405  
 L Y V L M V L G F F G F F T L G I M L S Y I R S K K L -71  
 GAGCACTCGAACGACCCATTCAACGTCTACATCGAGTCCGATGCCTGGCAAGAGAAGGACAAGGCCCTATGTCCAGGCCCGG-486  
 E H S N D P F N V Y I E S D A W Q E K D K A Y V Q A R -98  
 GTCCTGGAGAGCTACAGGTCGTGCTATGTCGTTGAAAACCATCTGGCCATAGAACAACCCAACACACACCTTCTGAGACG-567  
 V L E S Y R S C Y V V E N H L A I E Q P N T H L P E T -125  
 AAGCCTTCCCCATGAACCCCACTGGCTAAACTGGACACCTCCTGCTGGNNNNNAGATTTTCTAATCACATTCCTCTCA-648  
 K P S P \*  
 TACTCTTTATGTGATGGATACCACTGGATTTCTTTTTGGCTGTTGTAANGGTGAGGGGTGGATTAAATGACACTGTTTCA-729  
 CTGTTTCTCTAAATCACGTTCTTTTGTGATAGACTGTCAGTGGTTCCCCCATATCTGTCCCTGCCCTGCTAAATTTAGCA-810  
 GAATCCCTGAGGACATGGCCTCTGAGAATAGCAGCTATTTCACAGCTCCCTTGACGCTAGCAAGGTGTGTGACTAAG-891  
 CCTGGCCAGTAGGCATGGAAGTGAAGACTGTAATGTCCAAGTAATCCTTGGAAAGAAAAGAACGTGCCCTTAACCTA-972  
 TGTCTGCTTCCAGTGGCTGGATGTGGAGGAGGTGGAGACAGTTATGAGACTGGGAAAGTTCGGGGCACTCAAAGAGCC-1053  
 ACACACATCTGGGCTGGGCGACGTGGATCCTCCTTACCACCCACCAGGCCAGATTTACAGGAGAGAGAAATCCACTCCAC-1134  
 TCTTCTTAAGCCACTGTTATTCTGATCTCTGTTAAGGTGCGAGAATCAATGCCCTTACTGATACACCTACCTTATAGGAC-1215  
 TGAACCTAAAGGCATGACATTTCCATACTTGTGCACAGCACACACTGATTCTGCCCTTGTCACTTCTGTGCTCACTCTTGT-1296  
 GGCTCTATCCTCCTCCTGCCCTTCCGCCTTCCACTCCTCCCTTGCACCCATCCTGCACACATCTCCCTGAAAACACACAGG-1377  
 CACATACACTCATATACATAGACACACATACACCTCAATCTAGAAAGAACTTGCTTTGTACAGGGCTGAGATGGAGGAG-1458  
 AAAAAAATGCCCCCTTCAAGATGCATACCAAGGGGAAGGTGCTCGGTCACTGTGGGAGCAGGGAAGGTGCCCCCACTCCC-1539  
 CGAGAGCCAGGGGAAGGAGTGGCTCTGGGCAGAGAGGGACACATAGCACTGGGGTGGCAGGTCTTTTGAGGTGATGGGCC-1620  
 GGTTTTGTGAGATGAATTGTATCCCCCAAAAAGACAGGTACCTTCAATGTGACCTAATTGGGAAATAGAGTCTTTGCAGAT-1701  
 G(A)n -1702

Figure 18